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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/079,758	05/15/98	MORRISON D	MSC-22939-1-

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1616	7

DATE MAILED: 12/22/99

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/079,758	Morrison et al
Examiner	**Group Art Unit**
Shahnam Sharareh	1616

☒ Responsive to communication(s) filed on *5/15/98, 10/25/99*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-59 and 69-71* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-59 and 69-71* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

The amendment filed on October 25, 99 has been entered. Accordingly, claims 1, 3-5, 69, and 71 have been amended. Further, the restriction requirement is deemed proper as discussed in Paper No. 5, and is therefore made FINAL. Thus, claims 1-59, and 69-71 are pending in this application. Claims 60-68 stand withdrawn.

Claim Rejections - 35 USC § 112

1. The amended claims overcome the rejections made under 35 USC § 112.

2. The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

3. Claims 2-4 rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The instant claims are vague with regard to their respective recitations of an energy source. The recitation of " the enrgy source is a magnetic field, or radiofrequency or ultrasound" does not further limit the structure of the claimed microcapsule.

Priority

2. Applicant's arguments in regard to the effective priority date was considered, but were not found persuasive. Examiner would like to point out that the U.S. application Serial No. 08/349,169 filed December 2, 1994, now US Patent 5,827,531 fails to teach specific features of

the instant claims. For example, there are no teaching in the patented application with regard to energy absorbing components such as graphite, aluminum powder or Tween in contact with the outer membrane of the instant microcapsule, wherein said energy absorbing component is capable of melting at least a portion of the polymer membrane. In addition there are no teachings of said microcapsule comprising a drug or drug precursor. Further, Examiner was unable to locate the discussed teachings in the parent application as pointed out by Applicant in page 4 of Paper No.6. Thus, the effective priority date used for the examination of the instant application is still May 15, 1998.

Claim Rejections - 35 USC § 102

3. Applicant's arguments with regard to the rejection made under 35 U.S.C. 102(b) as being anticipated by Mathiowitz et al US Patent 4,898,734, or Radhakrishnan US Patent 5,049,389 have been fully considered and are found persuasive, therefore, said rejections are withdrawn.

4. Applicant's arguments with regard to the rejection made under 35 U.S.C. 102(e) as being anticipated by Unger et al US Patent 5,852,752 have been fully considered but are not persuasive. Applicant argument is on the basis that Unger et al do not teach an energy absorbing component that is specifically heated to a temperature beyond the melting point of the outer membrane by the absorption of energy. In response Examiner states that the independent claim 1 recites a limitation for the function of an energy absorbing component which does not cause a structural difference between the claimed invention and the prior art. Unger et al specifically disclose the incorporation of metal ions bound to lipid head groups which inherently act as an energy

absorbing component, and further when exposed to thermal stimulation will form reactive oxygen intermediates on the outer membrane, thus disrupting the membrane integrity to facilitate drug release (see col 38 lines 1-13.) Similarly, Unger states that ultrasound may be utilized not only to rupture but also to cause thermal effects which may increase the rate of the release of the active drug (see col 38 lines 28-31.) In addition, not only Unger et al disclose the incorporation of metal oxides in their liposomes that can act as an energy absorbing component (see col 23 lines 35-39.), but also various types of emulsifying agents such as various oils, various polysorbates (Tweens), and sorbitan derivatives such as sorbitan monooleate (see col 23 lines 40-66.), all of which according to the instant application, can act as the energy absorbing component for the compositions of Unger et al. Further, Applicant's assertion that the rupture of the Unger liposomes is governed by the makeup of the liposomal membrane and the gaseous precursor, is not impressive because the instant claims are directed to microcapsules comprising an energy absorbing component, not a specific resonant frequency at which such composition may rupture.

The independent claims of the instant application are drawn to microcapsules comprising one or more internal containing immiscible liquid phases, an outer polymer membrane, one or more energy absorbing components in an internal liquid phase; a magnetic particle, a drug or drug precursor, and further said microcapsules are in a pharmaceutically acceptable solution. The instant claims are also drawn to methods of delivering said microcapsule comprising administering the drug delivery solution to a subject and exposing the microcapsule to an energy source.

Unger disclose a liposome for controlled drug delivery of pharmaceutically active agents utilizing an energy source (see col 25 lines 17-22, col 40 lines 20-29) comprising one or more internals (see col 21 lines 18-20); an outer polymer membrane comprising groups (see col 20 line 46-67, col 21 & 22); an emulsifying agent such as TWEEN or sorbitan monooleate; an suspending agent such as glycerol, alginate, aluminum monosterate, aluminum silicate (see col 23 lines 39-66 and col 25 lines 59-67); a paramagnetic particle (see col 33 lines 46-55); various drug or drug precursors selected from therapeutic classes such as antibiotics, anti cancer, antiinflammatory, antifungal (col 32 lines 37-60, col 33 lines 46-67, col 34-35), in variety of sizes (see col 27 lines 11-41) delivered to specific sites via a pharmaceutically acceptable solution (see col 26 lines 3-30). Unger et al also disclose methods of delivering said microcapsule comprising administering the drug delivery solution to a subject and exposing the microcapsule to an energy source (see col 27 lines 56-65, col 40 lines 20-30). Therefore, the rejection is adhered to.

4. Applicant's arguments with respect to the rejected made under 35 U.S.C. 103(a) have been considered but are moot in view of the new ground(s) of rejection.

5. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 1-43, 69-71 rejected under 35 U.S.C. 102(b) as being anticipated by Grinstaff et al US Patent 5,498,421.

The independent claims of the instant application are drawn to microcapsules comprising one or more internal containing immiscible liquid phases, an outer polymer membrane, one or more energy absorbing components in an internal liquid phase, a drug or drug precursor, and further said microcapsules are in a pharmaceutically acceptable solution.

Grinstaff et al teaches a polymeric shell for delivery of biologicals comprising an outer polymer membrane, an energy absorbing component such as metal particles selected from the group consisting of iron, iron oxide, and manganese; a biocompatible dispersing agent such as soybean oil, corn oil, cotton seed oil, a drug selected from various therapeutic classes, in a pharmaceutically acceptable carrier (see abstract, col 8 lines 1-55, col 14 lines 26-36, col 25 lines 1-21.) Therefore, Grinstaff et al meet the limitations set forth in the instant claims

6. Claims 1, 3-9, 11, 21-23, 31-35, 40-43 rejected under 35 U.S.C. 102(b) as being anticipated by McGinity et al US Patent 5,288,502.

The independent claims of the instant application are drawn to microcapsules comprising one or more internal containing immiscible liquid phases, an outer polymer membrane, one or more energy absorbing components in an internal liquid phase, a drug or drug precursor, and further said microcapsules are in a pharmaceutically acceptable solution.

McGinity et al disclose multi-phase polymeric microspheres containing molecular compound dispersed in a polymeric matrix (see abstract.) McGinity's microsphere has a diametere of between 50 micron to 200 micron and comprises biocompatible polymer that surrounds a fixed oil, wherein the fixed oil contains a drug (see claims 1-11, 19.) More

specifically, the internal of the microsphere of McGinity contains two liquid immiscible phase comprising Tween 80 (which inherently possess energy absorbing properties), aluminum monosterate (see col.15,table1,and lines 54-64.) McGinity also disclose various types of drugs that can be incorporated into their microspheres such as various anticancer proteins (TNF, interferon) or antithromobotic agent (urokinase). Therefore, McGinity et al meet the limitations set forth in the instant claims.

7. Claims 1-4, 6-8, 21, 24, 26-27, 36, 40-44, 69-71 rejected under 35 U.S.C. 102(b) as being anticipated by Tsuei et al US Patent 5,589,194.

The instant claims are drawn to microcapsules comprising one or more internal containing immiscible liquid phases, an outer polymer membrane, one or more energy absorbing components in an internal liquid phase, a magnetic particle, a drug or drug precursor, and further said microcapsules are in a pharmaceutically acceptable solution. The instant claims are also drawn to methods of delivering said microcapsule comprising administering the drug delivery solution to a subject and exposing the microcapsule to an energy source.

Tsuei et al disclose microcapsules.comprising an outer polymer membrane, an energy absorbing component, and a drug (see abstract, claim 17) Tsuei also disclose the incorporation of various fillers such as graphite and energy absorbing particles in their microcapsules (see col 5 lines 29-37, col 6 lines 50-65.) Tsuei further disclose methods of releasing the active drug from the microcapsule core comprising applying energy so that the energy absorbed by the energy absorbing components of their microcapsule can further melt the outer membrane thereby

releasing the active component (see col 10 lines 20-25.) Therefore, Tsuei et al meet the limitations set forth by the instant claims.

Claim Rejections - 35 USC § 103

8. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

9. Claims 1-59, and 69-71 are rejected under 35 U.S.C. 103(a) as being unpatentable over Tsuei et al US Patent 5,589,194, and Unger et al US Patent 5,853,752,

The instant claims are drawn to microcapsules comprising one or more internal containing immiscible liquid phases; an outer polymer membrane comprising groups such as glycerol monosterate, cholesterol, polyvinyl alcohols or lecithins; one or more energy absorbing components in an internal liquid phase, such as graphite, TWEEN, or an oil in contact with the outer membrane; a magnetic particle; a drug or drug precursor wherein said drug or drug precursor is an antibiotic, an anti-cancer drug, an antifungal, an anesthetic, an antiviral, a thrombolytic agent, or an antiinflammatory; and further said microcapsules are in a pharmaceutically acceptable solution.

Microspheres and liposomes are readily used in pharmaceutical industry as a drug delivery vehicle Tsuei, and Unger teach the methods of making and the methods of utilizing microspheres

or liposomes in drug delivery systems. Thus, the teachings of Tsuei et al and Unger are viewed as being in the same field of endeavor.

Although Tsuei et al do not specifically teach the incorporation of various types of anticancer, antibiotics or radiocontrast agents in their compositions, they suggest the use of various pharmaceuticals and radiocontrast agents in their composition, therefore, it would have been obvious to one of ordinary skill in the art to develop a microcapsule comprising various types of pharmaceutical agents as taught by Unger et al to create microcapsules that can deliver a desired therapeutic agent to a specific site. Further, although Tsuei et al do not specifically teach methods utilizing various energy sources, they suggest the use of external energy source for releasing the active drug from their microcapsules, therefore, it would have been obvious to one ordinary skilled in the art to apply various types of energy sources taught by Unger et al to enhance the delivery of a therapeutic agent of choice.

New Matter

Claims 69-71 rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. The recitation of "compositions comprising at least two groups of microcapsules, wherein a first group has a polymer outermembrane with a different melting point than microcapsules of a second group, and further wherein both first and second melting points are lower than the Curie point of the magnetic particles" is not supported in the disclosure.

Conclusion

No claims were allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Shahnam Sharareh, PharmD whose telephone number is (703) 306-5400. The examiner can normally be reached on Monday to Friday from 8:30 a.m. to 5:00 p.m. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Mr. Jose Dees can be reached on 703-308-4628. The fax phone number for this Group is 703-308-4556. Any inquiry of a general nature of relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is 703-308-1235.

sjs, 12/12/ 1999

JOSE' G. DEES
SUPERVISORY PATENT EXAMINER
1616